Environmental Health Perspectives
Vol. 48, pp. 93-97, 1983

Epidemiologic Approaches to Persons with Exposures to Waste Chemicals

by Philip J. Landrigan*

Evaluation of disease in populations exposed to hazardous waste dumps requires: documentation of the chemicals in a dump; assessment of the materials released from the dump into environmental media; tracing of the probable routes of human exposure (groundwater, air, direct contact, or occupational); development, when possible, of individual exposure estimates and/or direct biological assessment of absorption; precise definition of the subpopulations at highest risk of exposure; and the employment of specific and sensitive health outcome indicators. Demonstration of dose-response relationships between chemical exposure and disease provides the most compelling evidence for a chemical etiology of illness in exposed populations. Interpretation of apparently negative data must be cautious, given the small size of most high-risk populations and the usual brevity of exposures.

Introduction

Since 1958, 750 million tons of waste chemicals have been discarded in the United States by the chemical manufacturing industry (*1*). The disposal of these materials has until recently been neither responsibly controlled by industry nor sufficiently regulated by government. In consequence, chemical wastes have been dispersed widely in the environment and have accumulated across the nation in some 30,000 to 50,000 disposal sites (*2*).

The persons exposed to toxic chemicals at dump sites have included workers—both those workers employed in routine operations as well as firefighters, police and members of special disposal squads who must enter dumps when there are unexpected spills, explosions or fires (*3*). Persons living or working in communities adjacent to dumps are also at risk of exposure, albeit usually at lower doses. Their exposures may result from inhalation of dusts or fumes dispersed from dumps (*4*) or from ingestion of wastes which have leached from dumps into drinking water (*5,6*).

Health effects of exposures to chemical dump sites may occasionally be acute and overwhelming, as for emergency workers who may suffer serious respiratory impairment as the result of toxic smoke inhalation during dump fires (*7*). More typically, however, exposures are less dramatic, and any resulting illnesses will tend to be subtle, insidious and delayed in their onset.

The evaluation of dysfunction or disease in persons exposed to chemical dumps requires both clinical acumen and biochemical sophistication. Yet no evaluation, however technically sophisticated, will be successful if it examines the wrong groups of persons or if it fails to ascertain as precisely as possible the chemicals and the mixtures to which persons have been exposed.

The function of epidemiology in the evaluation of persons exposed to chemical dumps is to document and to define any etiologic associations which may exist between exposure and disease. Epidemiology in this context is the discipline which guides study design. It facilitates exploitation of the quasi-experiment which results from the exposure of a population to toxic waste chemicals.

*Division of Surveillance, Hazard Evaluations and Field Studies, National Institute for Occupational Safety and Health, Centers for Disease Control, 4676 Columbia Parkway, Cincinnati, OH 45226.

In this paper, I shall outline several of the basic epidemiological tenets which ought to guide the evaluation of persons exposed to chemical dumps. In essence, there are four such principles: (1) that the nature and extent of exposure must be documented; (2) that the exposed populations must be precisely defined; (3) that disease and dysfunction in the exposed populations must be diagnosed as unequivocally as possible; and (4) that the relationships between exposure and disease must be evaluated with rigorous statistical methodology in which particular attention is paid to the detection of any dose-response relationships.

Documentation of Exposure

The first requirement for evaluation of persons exposed to chemical wastes is accurate documentation of their exposure. Several points need to be considered in this documentation. An inventory must be developed of the materials contained in a dump. That catalog can be constructed either through review of past records or through sampling of the dump itself. The possibility must be borne in mind that interactions may have occurred among the discarded materials in the dump and that compounds may have formed which are more highly toxic than those originally deposited.

The nature and quantity of the major environmental emissions from a dump must be determined. Expert consultation may be required from hydrogeologists and from meteorologists to plot the movement of pollutants in water and in air. The utility of such pollutant mapping is well illustrated in a study of exposure to phenol in well water which was conducted in 1974 and 1975 by the Centers for Disease Control (*6*). In that situation, exposure resulted from a railroad accident in which 37,900 liters of 100% phenol were spilled on the ground from an overturned tank car. The phenol percolated into the soil, and over several weeks it migrated into groundwater and thence into the home wells of nearby families. Analysis of water samples from nearby wells enabled accurate plotting of the extent of the spill (Fig. 1) and made possible the accurate definition of the population at risk.

The probable routes of human exposure must be determined. For workers on dumps, inhalation will be the principal mode of exposure, and transcutaneous absorption may occasionally occur. In the members of adjacent communities, exposure may occur either through inhalation or through consumption of contaminated water. Community residents may also on occasion be exposed to waste chemicals through direct contact, as were the children near Love Canal who drove their bicycles over piles of discarded Lindane.

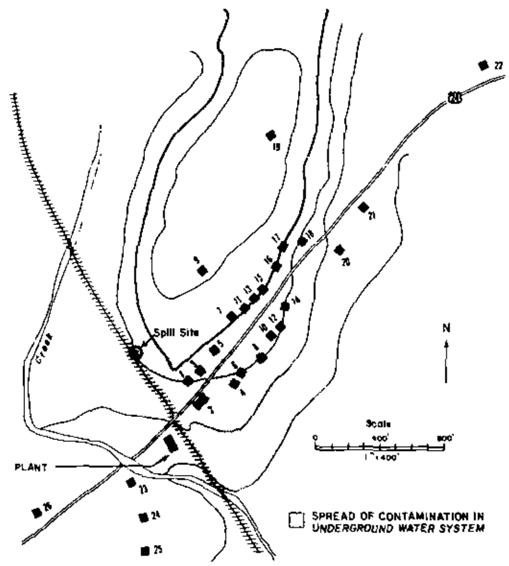

FIGURE 1. Location of phenol contamination, Walworth County, Wisconsin, 1974–1975.

Estimates of human exposure must be developed. These estimates should consider both the daily dose received by members of the exposed population and also the duration of exposure. In some instances, it may be possible to estimate total time-integrated exposure to chemical contaminants (*8*). The most useful exposure estimates are those which are specific for each individual in a population. Among dump workers, for example, measurement of individual breathing zone airborne exposures by means of personal air sampling pumps provides much more specific information than does collection of area air samples using stationary monitors; the latter approach, because it overlooks individual variations in exposure and averages out differences, may overlook significant associations between exposure and disease (*9*). Similarly, in the evaluation of exposure to waterborne contaminants, individual exposure estimates based on individual water consumption histories are potentially much more valuable than grouped data. For example, in a study of exposure to arsenic in drinking water, which was conducted several years ago by the Alaska Division of Public Health and the Centers for Disease Control, simple measurement of the concentration of arsenic in home well water was found to be a surprisingly poor indicator of individual exposure (*10*). However, when detailed histories were taken, it was learned that following a public debate over the possible harmful health effects of arsenic, many persons had stopped drinking water from their wells and had substituted bottled water. When the exposure data from the persons drinking bottled water were properly considered and the correlation between arsenic exposure and actual well water consumption then recomputed, a much more highly positive dose-effect correlation was demonstrated (*10*).

Estimates of external exposure may on occasion be complemented by biological sampling in which more direct measurement is made of the body burden of a toxic chemical or of the amount excreted. Determinations of serum and breast milk concentrations of polybrominated biphenyls (PBB) (*11*) and of urinary concentrations of arsenic (*10*) have, for example, enabled reasonable estimates to be made of individual exposures in populations exposed to those chemicals.

Definition of Exposed Populations

The second requirement for documentation of the health effects of exposure to chemical dumps is precise definition of the populations at risk. Such definition depends entirely upon the quality and completeness of occupational monitoring and environmental mapping. A useful concept in the definition of exposed populations may be the identification of the "critical" or most heavily exposed population. In many instances, this group will be comprised of workers at a dump. Occasionally, however, the critically exposed population may be made up of those persons with the most heavily contaminated wells or those persons into whose cellars the contents of a landfill explode or those people who eat root vegetables grown on top of a landfill. Identification of such populations requires careful observation and a bit of ingenuity.

The major goal of accurate definition of the population at risk is to distinguish exposed persons from unexposed. In terms of a 2 × 2 table (Fig. 2), environmental mapping should be sufficiently precise such that all cases of disease in a population caused by toxic chemical exposure are confined to cell *a*. However, with an overly broad definition of the population at risk, cases of toxic illness may be distributed across cells *a* and *b*. Dilution of the association between exposure and disease results, and the causal connection may no longer be evident.

In epidemiologic studies of persons exposed to chemical dumps, it is most important that evaluations be precisely targeted. High risk groups (the critical population) may often be small in number, and the temptation to augment their size by combining them with less heavily exposed persons may be strong. That tendency should, however, be resisted, for it will dilute the data. The development of individual exposure estimates constitutes an excellent defense against such dilution.

		EXPOSURE	
		YES	NO
DISEASE	YES	a	b
	NO	c	c

FIGURE 2. Exposure vs. disease in relation to waste chemical dumps. With accurate environmental mapping and precise definition of the population at risk, any cases of toxic disease caused by exposure to waste chemicals will occur in cell *a*. With overbroad definition of the population at risk (dilution phenomenon), cases will be distributed across cells *a* and *b*, and the etiologic association between exposure and disease may no longer be detectable.

Documentation of Disease and Dysfunction

The medical evaluation of populations exposed to waste chemical dumps must also be precisely targeted. Physicians must resist the temptation to do complete physical examinations on all members of an exposed population in the hope that patterns will emerge. Instead, the examination must be pared down. It must seek specifically those adverse health effects, both clinical and subclinical, which are biologically plausible in terms of actual exposures. A sharp distinction must be made between the clinical approach to the individual patient and the evaluation of an exposed population. Flexibility and imagination are the keys to the former, but only rigorous standardization and a sharply delimited examination protocol will succeed in an investigation of the latter (*11*). In some clinical evaluations of persons exposed to waste chemicals, it may be useful to include unexposed or control groups and to blind the examiners in regard to the exposure status of each individual examined.

The clinical studies employed in the evaluation of populations exposed to chemical dumps must be both as specific and as sensitive as possible. In terms of the 2 × 2 table (Fig. 2), both the overdiagnosis of disease in unexposed persons as well as the underdiagnosis of illness in exposed persons must be minimized. The occurrence of serious misclassification in either direction can obscure etiologic associations.

Linkage of Exposure to Illness

Etiologic association between exposure and disease is most simply established in dichotomous fashion. In the 2 × 2 table (Fig. 2), this demonstration is accomplished by showing that there exists a statistically significant difference in the prevalence of disease among exposed members of a population as contrasted with the rate in the unexposed. This demonstration may be further refined by considering the time dimension; if there is a cause and effect association, disease should follow exposure, and not vice versa. Also the observed disease or dysfunction should be biologically plausible and compatible with the known or suspected toxic effects of the involved chemicals.

The most convincing evidence for the existence of a cause-effect relationship is provided by the demonstration of a dose-response relationship. The frequency and severity of disease should be expected to increase with the intensity or duration of exposure, and the absence of a dose-response relationship casts doubt on the validity of a reported association. The classic example of dose-response in an epidemiological study is provided by the investigations of lung cancer in relation to cigarette smoking by Doll and Hill. Doll and Hill found that the death rate from lung cancer among British physicians was significantly higher in smokers than in nonsmokers and that the rate increased sharply the more tobacco was consumed (*13,14*). Likewise, in studies of persons exposed to lead, the prevalence of anemia was found to be higher in exposed than in unexposed persons, and further, the concentration of hemoglobin in the blood of exposed persons was found to be rather precisely correlated with their blood lead levels; persons with higher blood lead levels had lower hemoglobin concentrations (*15*).

Negative Data

Health evaluations of persons living near waste dumps, even those evaluations which employ the most sophisticated test instruments, may frequently be expected to show no adverse health effects. Such negative data must, however, be evaluated very cautiously. It cannot be concluded from a single negative investigation or even from several apparently negative studies that no damage has occurred to the exposed populations. The following factors must be considered in the evaluation of apparently negative data: the size of the population, latency and study design.

The populations heavily exposed to waste dumps will frequently be small. Therefore, the statistical power of studies conducted in such groups will be low, and the studies will have difficulty in detecting cause-effect relationships, even if toxic disease is present. Many epidemiologists, our group included, now recommend that any negative epidemiologic report include a clear statement as to the statistical power of the study to detect a particular increased frequency of a given disease (*16*).

Chronic disease, cancer in particular, may develop only years or decades after the start of exposure. Frequently, no indication of impending disease will be present during the latency period, even though irreversible cellular damage may already have occurred. Thus studies done too soon after the start of exposure may fail to detect illness which has yet to develop. There is, therefore, an important role for registries and for prospective studies.

Finally, the importance of proper study design and of careful documentation of exposure cannot be overemphasized. Misclassification must be considered as a possible cause of any apparently negative environmental study (*9*). The additional possibility always exists that groups other than those most heavily exposed have been evaluated or that heavily and lightly exposed persons have been improperly combined with resultant dilution of the findings.

Recommendations

The major recommendation of this paper is rather self-evident: that future epidemiological studies be conducted with proper regard for the basic niceties of study design. Exposures must be measured; exposed groups must be defined and not diluted; control groups must be used where appropriate; diagnostic instruments must be precise.

There will be an increasing need in future studies of persons exposed to toxic waste chemicals for individual exposure measurements. Techniques, such as those used already in occupational studies, must be developed for the passive, unobtrusive and quantitative monitoring of individual exposures in community populations.

Finally, there is a societal need for the development of improved methods for tracing persons who have been exposed to toxic chemicals. The newly established National Death Index should be a great aid in this regard. Consideration might be given also to the establishment of federal statistical enclaves or to the practice of assigning unique identifying numbers to all persons in the population. Although profound ethical and societal issues will surround those decisions, the potential advantages which they will afford for development of medical knowledge of environmental exposures are enormous (*17*).

REFERENCES

1. Health Effects of Toxic Pollution: A Report from the Surgeon General. U. S. Government Printing Office, Washington, D. C., August 1980, Serial No. 95-16.

2. Hart, F. C. Preliminary Assessment of Clean-up Costs of National Hazardous Waste Problems. Report to the U.S. Environmental Protection Agency. EPA, Washington, D. C., February 23, 1979.
3. Landrigan, P. J., and Gross, R. L. Chemical wastes—illegal hazards and legal remedies. Editorial. Am. J. Publ. Health 71: 985-987 (1981).
4. Singal, M., Kominsky, J. R., Schulte, P. A., and Landrigan, P. J. Technical Assistance Final Report No. 79-022-789: Hyde Park Landfill, Niagara, NY. National Institute for Occupational Safety and Health, Cincinnati, 1980.
5. Trichloroethylene exposure - Pennsylvania. Morbidity Mortality Weekly Rept. 30: 226-233, May 22, 1981.
6. Baker, E. L., Field, P. H., Basteyns, B. J., Skinner, G. H., Bertozzi, P. E., and Landrigan, P. J. Phenol poisoning due to contaminated drinking water. Arch. Environ. Health 33: 89-94 (1978).
7. Halperin, W., Landrigan, P. J., Altman, R., Iaci, A. W., Morse, D. L., Needham, L. L. Chemical fire at a toxic waste disposal plant: epidemiologic study of exposure to smoke and fumes. J. Med. Soc. N. J. 78: 591-594 (1981).
8. Smith, A. H., Waxweiler, R. J., and Tyroler, H. A. Epidemiologic investigation of occupational carcinogenesis using a serially additive expected dose model. Am. J. Epidemiol. 112: 787-797 (1980).
9. Gladen, G., and Rogan, W. J. Misclassification and the design of environmental studies. Am. J. Epidemiol. 109: 607-616 (1979).
10. Harrington, J. M., Middaugh, J. P., Morse, D. L., and Housworth, J. A survey of a population exposed to high concentrations of arsenic in well water in Fairbanks, Alaska. Am. J. Epidemiol. 108: 377-385 (1978).
11. Landrigan, P. J., Wilcox, K. R., Silva, J., Humphrey, H. E. B., Kauffman, C., and Heath, C. W., Jr. Cohort study of Michigan residents exposed to polybrominated biphenyl: epidemiologic and immunologic findings. Ann. N. Y. Acad. Sci. 320: 284-294 (1979).
12. Rose, G. A., and Blackburn, H. Cardiovascular Survey Methods. World Health Organization, Geneva, 1968.
13. Doll, R., and Hill, A. B. A study of the etiology of carcinoma of the lung. Brit. Med. J. 2: 1271-1286 (1952).
14. Doll, R. Bronchial carcinoma: incidence and etiology. Brit. Med. J. 2: 521-527, 585-590 (1953).
15. Baker, E. L., Landrigan, P. J., Barbour, A. G., Cox, D. H. Folland, D. S., Ligo, R. N., and Throckmorton, J. Occupational lead poisoning in the United States: clinical and biochemical findings related to blood lead levels. Brit. J. Ind. Med. 36: 314-322 (1979).
16. Beaumont, J. J., and Breslow, N. Power considerations in the evaluation of epidemiologic studies of vinyl chloride workers. Am. J. Epidemiol. 114: 725-734 (1981).
17. Gordis, L., and Gold, E. Privacy, confidentiality and the use of medical records in research. Science 207: 153-156 (1980).